

TOPICAL HAZARD EVALUATION PROGRAM OF US DEPARTMENT OF AGRICULTURE CANDIDA..(U) ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GROUND MD J.V WADE ET AL.

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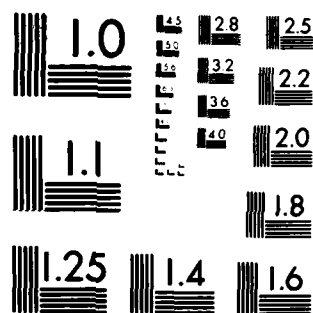
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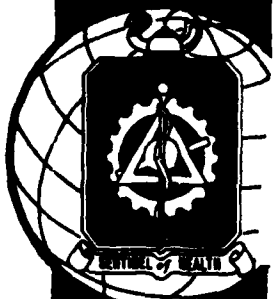
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010-5422

TOPICAL HAZARD EVALUATION PROGRAM
OF
US DEPARTMENT OF AGRICULTURE
CANDIDATE INSECT REPELLENT AI3-20784-Gc
[N,N-diethyl-d, l-mandelic acid amide (DEM)]
STUDY NO. 75-51-0486-84
NOVEMBER 1983 - APRIL 1984

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0486-84	2. GOVT ACCESSION NO. AD A144 337	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-20784-Gc, US Department of Agriculture Proprietary Chemical, Study No. 75-51- 0486-84, November 1983 - April 1984		5. TYPE OF REPORT & PERIOD COVERED Final, November 1983 - April 1984
7. AUTHOR(s) John V. Wade, DVM, CPT(P), VC John G. Harvey, Jr.		6. PERFORMING ORG. REPORT NUMBER
9. PERFORMING ORGANIZATION NAME AND ADDRESS Commander US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010-5422		8. CONTRACT OR GRANT NUMBER(s)
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Ft Sam Houston, TX 78234-6000		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Chemical AI3-20784-Gc (DEM) produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. It produced moderate injury to the cornea and, in addition, some injury to the conjunctiva upon application to the eyes of rabbits. Ocular injury noted was decreased by washing with water following application and was resolved in all test animals by seven days post-application. Chemical AI3-20784-Gc (DEM) did not produce sensitization or photochemical irritation and was relatively nontoxic upon ingestion. Recommend that chemical AI3-20784-Gc [N,N-diethyl-d, 1-mandelic acid amide (DEM)] be approved		

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20. for further testing as a candidate insect repellent if its entomological efficacy is superior to currently used repellents. This chemical should be used with extreme caution around the eyes and mucosal surfaces. Should the chemical be accidentally introduced into the eye, it should be flushed with copious amounts of water.

RE: Study No. 75-51-0486-84

Report does not contain proprietary information. The name is not given but the number is concerning insect propellant. Only the Dept. of Agriculture and AEHA know the name associated with the number.

Per Lt. Col. R. T. Callis, AEHA



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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

CPT(P) Wade/dlc/AUTOVON
584-3980

REPLY TO
ATTENTION OF

HSHB-OT/WP

2 AUG 1984

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
AI3-20784-Gc, N,N-diethyl-*d*, *l*-mandelic acid amide (DEM), Study
No. 75-51-0486-84, November 1983 - April 1984

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings, and major recommendations of the inclosed report follow:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-20784-Gc, N,N-diethyl-*d*, *l*-mandelic acid amide (DEM), by means of laboratory animal studies using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs.

b. Essential Findings. Chemical AI3-20784-Gc (DEM) produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. It produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva upon application to the eyes of rabbits. Occular injury noted was decreased by washing with water following application and was resolved in all test animals by 7 days postapplication. Chemical AI3-20784-Gc (DEM) did not produce sensitization or photochemical irritation and was relatively nontoxic upon ingestion.

c. Major Recommendation. Recommend that chemical AI3-20784-Gc (DEM) be approved for further testing as a candidate insect repellent if its entomological efficacy is superior to currently used repellents. This chemical should be used with extreme caution around the eyes and mucosal surfaces.

FOR THE COMMANDER:

1 Incl
as

Joel C. Gaydos
JOEL C. GAYDOS, M.D.
Colonel, MC
Director, Occupational and
Environmental Health

CF:
HQDA (DASG-PSP) w/o incl
Cdr, HSC (HSCL-P)
Comdt, AHS (HSHA-IPM)
Dir, Advisory Cen on Tox, NRC (2 cy)
USDA, ARS (DR. Terrence McGovern)
USDA, ARS-Southern Region (3 cy)
Cdr, USAMRDC [SGRD-DPM/LTC(P) Reinert]



DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO
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TOPICAL HAZARD EVALUATION PROGRAM
OF
US DEPARTMENT OF AGRICULTURE
CANDIDATE INSECT REPELLENT AI3-20784 Gc
[N,N-diethyl-d, l-mandelic acid amide (DEM)]
STUDY NO. 75-51-0486-84
NOVEMBER 1983 - APRIL 1984

1. AUTHORITY.

a. Letter, DOD, Armed Forces Pest Management Board, Forest Glen Section, WRAMC, Washington DC, 14 November 1983.

b. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 5 January 1984.

c. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations; titled Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Topical Hazard Evaluation Program Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), January 1982.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-20784-Gc (DEM).

4. SUMMARY OF FINDINGS. Hazard evaluation of the candidate insect repellent AI3-20784-Gc (DEM) was conducted by this Agency using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs. A tabular presentation of animal toxicity data developed by this Agency follows:*†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals"; US Department of Health, Education, and Welfare; Public Health Service; National Institutes of Health (NIH) Publication No. 80-23, revised 1978, reprinted April 1980.

† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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TABLE. PRESENTATION OF DATA

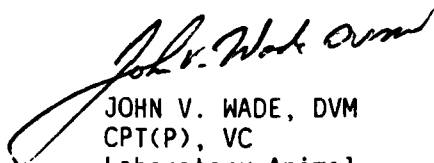
Test	Results	Interpretation
SKIN IRRITATION STUDIES		
Rabbits Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemical AI3-20784-Gc produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.	USAEHA Category II (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.		
EYE IRRITATION STUDIES		
Rabbits Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.	Chemical AI3-20784-Gc produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva. Washing with warm water decreased the ocular injury noted.	USAEHA Category E (ref Appendix A)
APPROXIMATE LETHAL DOSE (ALD)		
Oral Rats (male) - no diluent	ALD 2,222 mg/Kg	This chemical is relatively non-toxic by ingestion.
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits A single 0.05 mL application of a 25% (w/v) solution of AI3-20784-Gc and of a 10% (w/v) Oil of Bergamot solution (positive control) in 95% ethanol was applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.	Chemical AI3-20784-Gc did not produce photochemical irritation under test conditions.	This chemical is not expected to produce photochemical irritation in humans.

Test	Results	Interpretation
PHOTOCHEMICAL SKIN IRRITATION STUDIES (continued)		
Control Following UV exposure of the rabbits, 0.05 mL of the test chemical, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked at 24, 48, and 72 hours.	Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	
SENSITIZATION STUDIES		
Guinea Pigs (female) Intradermal (ID) injections of 0.1 mL of a 1.0% (w/v) solution of chemical AI3-20784-Gc or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with ID injections of the test chemical.	Challenge dose of chemical AI3-20784-Gc did not produce a sensitization reaction.	This chemical is not expected to produce sensitization in humans.
Control Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After a 2-week rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a moderate to marked sensitization reaction in 9 out of 10 guinea pigs.	DNCB produced a sensitization reaction, indicating that these guinea pigs respond to sensitizing agents.

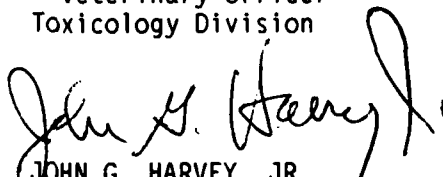
* A known skin sensitizer.

5. CONCLUSION. Chemical AI3-20784-Gc (DEM) produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. It produced moderate injury to the cornea and, in addition, some injury to the conjunctiva upon application to the eyes of rabbits. Ocular injury noted was decreased by washing with water following application and was resolved in all test animals by 7 days postapplication. Chemical AI3-20784-Gc (DEM) did not produce sensitization or photochemical irritation and was relatively nontoxic upon ingestion. These studies were monitored by Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that chemical AI3-20784-Gc [N,N-diethyl-d, l-mandelic acid amide (DEM)] be approved for further testing as a candidate insect repellent if its entomological efficacy is superior to currently used repellents. This chemical should be used with extreme caution around the eyes and mucosal surfaces. Should the chemical be accidentally introduced into the eye, it should be flushed with copious amounts of water.



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APPROVED:



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APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following:

a. These studies were conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations (CFR), 1983 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

(3) Final Rule, Pesticide Programs; Good Laboratory Practice Standards; 48 Federal Register (FR) 53963-53969, 29 November 1983.

b. Facilities were inspected during its operational phase to ensure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting these studies.



PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office

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